

PHARMACOLOGY-III
UNIT-II
TOPIC: GENERAL PRINCIPLE OF
CHEMOTHERAPY



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General principles of chemotherapy

This type of therapy is generally called chemotherapy which has come to mean 'treatment of systemic infections with specific drugs that selectively suppress the infecting microorganism without significantly affecting the host.' The basis of selective microbial toxicity is the action of the drug on a component of the microbe (e.g. bacterial cell wall) or metabolic processes (e.g. folate synthesis) that is not found in the host, or high affinity for certain microbial biomolecules (e.g. trimethoprim for bacterial dihydrofolate reductase). Due to analogy between the malignant cell and the pathogenic microbes, treatment of neoplastic diseases with drugs is also called

'chemotherapy'.

Antibiotics These are substances produced by microorganisms, which selectively suppress the growth of or kill other microorganisms at very low concentrations.

Antimicrobial agent (AMA) to designate synthetic as well as naturally obtained drugs that attenuate microorganisms.

CLASSIFICATION

Antimicrobial drugs can be classified in many ways:

A. Chemical structure

1. Sulfonamides and related drugs: Sulfadiazine and others, Sulfones-Dapsone (DDS), Paraaminosalicylic acid (PAS) .
2. Oiaminopyrimidines: Trimethoprim, Pyrimethamine.
3. Quinalones: Nalidixic acid, Norfloxacin, Ciprofloxacin, Gatifloxacin, etc.
4. β -Lactam antibiotics: Penicillins, Cephalosporins, Monobactams, Carbapenems.
5. Tetracyclines: Oxytetracycline, Doxycycline, etc.
6. Nitrobenzene derivative: Chloramphenicol:
7. Aminoglycosides: Streptomycin, Gentamycin, Amikacin, Neomycin, etc.
8. Macrolide antibiotics: Erythromycin, Clarithromycin, Azithromycin, etc.
9. Lincosamide antibiotics: Lincomycin, Clindamycin.
10. Glycopeptide antibiotics: Vancomycin, Teicoplanin.
11. Oxazolidinone: Linezolid.
12. Polypeptide antibiotics: Polymyxin-B, Colistin, Bacitracin, Tyrothricin.
13. Nitrofuran derivatives: Nitrofurantoin, Furazolidone.
14. Nitroimidazoles: Metronidazole, Tinidazole etc.

15. Nicotinic acid derivatives: Isoniazid, Pyrazinamide, Ethionamide.

16. Polyene antibiotics. Nystatin, Amphotericin-B, Hamycin. 17. Azole derivatives: Miconazole, Clotrimoxazole, Ketoconazole, Fluconazole.

18. Others: Rifampin, Spectinomycin, Cycloserine, Viomycin, Ethambutol, Thiacetazone, Clofazimine, Griseofulvin.

B. Mechanism of action

1. Inhibit cell wall synthesis: Penicillin, Cephalosporins, Cycloserine, Vancomycin, Bacitracin.

2. Cause leakage from cell membranes: Poly-peptides-Polymyxins, Colistin, Bacitracin, Polyenes-Amphotericin B, Nystatin, Hamycin.

3. Inhibit protein synthesis: Tetracycline, Chloramphenicol, Erythromycin, Clindamycin, Linezolid.

4. Cause misreading of mRNA code and affect permeability: Aminoglycosides-Streptomycin, Gentamicin, etc.

Inhibit DNA gyrase: Fluoroquinolones Ciprofloxacin and others.

Interfere with DNA function: Rifampin, Metronidazole.

- Interfere with DNA synthesis: Acyclovir, Zidovudine.

- Interfere with intermediary metabolism: Sulfonamides, Sulfones, PAS, Trimethoprim, Pyrimethamine, Ethambutol.

◆ Type of organisms against which primarily active

1. Antibacterial: Penicillins, Aminoglycosides, Erythromycin, etc.

2. Antifungal: Griseofulvin, Amphotericin B, Ketoconazole, etc.

3. Antiviral: Acyclovir, Amantadine, Zidovudine, etc.

4. Antiprotozoal: Chloroquine, Pyrimethamine, Metronidazole, Diloxanide, etc.

5. Anthelmintic: Mebendazole, Pyrantel, Niclosamide, Diethyl carbamazepine, etc.

D. Spectrum of activity

Narrow-spectrum

Penicillin G, streptomycin

Broad-spectrum

Tetracyclines

Chloramphenicol

Hypersensitivity reactions

Practically all AMAs are capable of causing hypersensitivity reactions. These are unpredictable and unrelated to dose. The whole range of reactions from rashes to anaphylactic shock can be produced. The more commonly involved AMAs are-penicillins, cephalosporins, sulfonamides, fluoroquinolones.

Drug resistance

It refers to unresponsiveness of a microorganism to an AMA, and is akin to the phenomenon of tolerance seen in higher organisms.

Natural resistance Some microbes have always been resistant to certain AMAs. They lack the metabolic process or the target site which is affected by the particular drug.

Acquired resistance It is the development of resistance by an organism (which was sensitive before) due to the use of an AMA over a period of time.

Superinfection (Suprainfection) infection occurring after or on top of an earlier infection, especially following treatment with broad-spectrum antibiotics This refers to the appearance of a new infection as a result of antimicrobial therapy.

Use of most AMAs causes some alteration in the normal microbial flora of the body. The normal flora contributes to host defence elaborating substances called bacteriocins which inhibit pathogenic organisms. Further pathogen has to compete with the normal flora for nutrients, etc. to establish itself

Superinfections are more common when the defence is compromised.

- Corticosteroid therapy
- Leukaemias and other malignancies, especially when treated with anticancer drugs
- Acquired immunodeficiency syndrome (AIDS)
- Agranulocytosis
- Diabetes, disseminated lupus erythematosus